

Amendments to the Specification:

Please replace the paragraph beginning at page 15, line 8, with the following rewritten paragraph:

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In addition to commercially available kits for generating phage display libraries (e.g. the Pharmacia *Recombinant Phage Antibody System*, catalog no. 27-9400-01; and the Stratagene ~~SurfZAP~~TM SURFZAPTM phage display kit, catalog no. 240612), examples of methods and reagents particularly amenable for use in generating the variegated peptide display library of the present invention can be found in, for example, the Ladner et al. U.S. Patent No. 5,223,409; the Kang et al. International Publication No. WO 92/18619; the Dower et al. International Publication No. WO 91/17271; the Winter et al. International Publication WO 92/20791; the Markland et al. International Publication No. WO 92/15679; the Breitling et al. International Publication WO 93/01288; the McCafferty et al. International Publication No. WO 92/01047; the Garrard et al. International Publication No. WO 92/09690; the Ladner et al. International Publication No. WO 90/02809; Fuchs et al. (1991) *Bio/Technology* 9:1370-1372; Hay et al. (1992) *Hum Antibod Hybridomas* 3:81-85; Huse et al. (1989) *Science* 246:1275-1281; Griffiths et al. (1993) *EMBO J* 12:725-734; Hawkins et al. (1992) *J Mol Biol* 226:889-896; Clackson et al. (1991) *Nature* 352:624-628; Gram et al. (1992) *PNAS* 89:3576-3580; Garrad et al. (1991) *Bio/Technology* 9:1373-1377; Hoogenboom et al. (1991) *Nuc Acid Res* 19:4133-4137; and Barbas et al. (1991) *PNAS* 88:7978-7982. These systems can, with modifications described herein, be adapted for use in the subject method.

Please replace the paragraph beginning at page 39, line 11, with the following rewritten paragraph:

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The marker gene may also be a screenable gene. The screened characteristic may be a change in cell morphology, metabolism or other screenable features. Suitable markers include beta-galactosidase (X-gal, C12FDG, Salmon-gal, Magenta-Gal (latter two from Biosynth Ag)), alkaline phosphatase, horseradish peroxidase, exo-glucanase (product of yeast *exb1* gene; nonessential, secreted); luciferase; bacterial green fluorescent protein; (human placental) secreted alkaline phosphatase (SEAP); and chloramphenicol transferase (CAT). Some of the above can be engineered so that they are secreted (although not beta-galactosidase). A preferred

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screenable marker gene is beta-galactosidase; yeast cells expressing the enzyme convert the colorless substrate X-gal into a blue pigment. Again, the promoter may be receptor-induced or receptor-inhibited.

Please replace the paragraph beginning at page 43, line 23, with the following rewritten paragraph:

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As used herein, "variegated" refers to the fact that a population of peptides is characterized by having a peptide sequence which differ from one member of the library to the next. For example, in a given peptide library of n amino acids in length, the total number of different peptide sequences in the library is given by the product of $\{v_1 \times v_2 \times \dots \times v_{n-1} \times v_n\}$ where each v_n represents the number different amino acid residues occurring at position n of the peptide. In a preferred embodiment of the present invention, the peptide display collectively produces a peptide library including at least 96 to 107 different peptides, so that diverse peptides may be simultaneously assayed for the ability to interact with the target protein.

Please replace the paragraph bridging page 49 and page 50, with the following rewritten paragraph:

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In one embodiment the target receptor is a cytokine receptor. Cytokines are a family of soluble mediators of cell-to-cell communication that includes interleukins, interferons, and colony-stimulating factors. The characteristic features of cytokines lie in their functional redundancy and pleiotropy. Most of the cytokine receptors that constitute distinct superfamilies do not possess intrinsic protein tyrosine kinase domains, yet receptor stimulation usually invokes rapid tyrosine phosphorylation of intracellular proteins, including the receptors themselves. Many members of the cytokine receptor superfamily ~~activate~~ activate the Jak protein tyrosine kinase family, with resultant phosphorylation of the STAT transcriptional activator factors. IL-2, IL-7, IL-2 and Interferon γ have all been shown to activate Jak kinases (Frank et al (1995) *Proc Natl Acad Sci USA* 92:7779-7783); Scharfe et al. (1995) *Blood* 86:2077-2085); (Bacon et al. (1995) *Proc Natl Acad Sci USA* 92:7307-7311); and (Sakatsume et al (1995) *J. Biol Chem* 270:17528-17534). Events downstream of Jak phosphorylation have also been elucidated. For example, exposure of T lymphocytes to IL-2 has been shown to lead to the phosphorylation of

signal transducers and activators of transcription (STAT) proteins STAT1 α , STAT2 β , and STAT3, as well as of two STAT-related proteins, p94 and p95. The STAT proteins were found to translocate to the nucleus and to bind to a specific DNA sequence, thus suggesting a mechanism by which IL-2 may activate ~~speifie~~ specific genes involved in immune cell function (Frank et al. *supra*). Jak3 is associated with the gamma chain of the IL-2, IL-4, and IL-7 cytokine receptors (Fujii et al. (1995) *Proc Natl Acad Sci* 92:5482-5486) and (Musso et al (1995) *J Exp Med.* 181:1425-1431). The Jak kinases have also been shown to be activated by numerous ligands that signal via cytokine receptors such as; growth hormone and erythropoietin and IL-6 (Kishimoto (1994) *Stem cells Suppl* 12:37-44).

Please replace the paragraph beginning at page 63, line 12, with the following rewritten paragraph:

To test each of the plasmids, *E. coli* were transformed with the negative control pLITMUS plasmid and the Myc epitope-6xHis encoding plasmids: pAM6, pAM7 and pAM8. The cells were grown at 37°C to log phase and induced with 0.1 mM IPTG for 3 hours (+) or grown for 3 hours in the absence of IPTG (-). Whole cell lysates were separated by electrophoresis on a 16% tricine ~~SDS-PAG~~ SDS-PAGE, and immunoblotted with anti-myc antibody.

Please replace the paragraph beginning at page 64, line 13, with the following rewritten paragraph:

Phagemids produced as described above were also tested for titration of plaque and colony forming units generated upon phagemid rescue by ~~serially~~ serial dilution and infection into log phase *E. coli*. See Figure 11. Infected cells were either plated on soft agar to detect plaque forming units (p.f.u.), or on ampicillin to determine colony forming units (c.f.u.). c.f.u. represent those phage which have packaged a plasmid DNA, whereas p.f.u. represent phage which have packaged a helper a phage genome DNA.

Please replace the paragraph bridging page 64 and page 65, with the following rewritten paragraph:

Figure 13 shows an anti-pIII western blot detection of peptides incorporated into M13 phagemid capsids as pIII fusions. Briefly, oligonucleotides encoding the the Myc epitope-6xHis peptide, a thrombospondin derived peptide (tsp: SPWSSASVTCGDGVITRIR, SEQ ID NO: 7), an $\alpha v \beta 3$ integrin binding peptide containing the RGD motif (CDCRGDCFC, SEQ ID NO: 8) and the first kringle domain of angiostatin (K1: 80 amino acids) were inserted between the the BstXI sites of pAM9. In *E. coli*, the plasmids direct the expression of the peptide-pIII fusion proteins. For phagemid production the cells were grown at 37°C to log phase, induced with 0.1 mM IPTG, infected with M13 helper phage or an M13 helper phage that carries an amber mutation in the pIII gene and grown overnight. Phagemids contained in the culture media supernatant were separated by electrophoresis on a 16% tricine ~~SDS-PAGE~~ SDS-PAGE, and immunoblotted with anti-pIII antibody. As a control M13K07 phage particle were used. The lower bands correspond to wild type pIII proteins while the upper, higher molecular weight bands correspond to the peptide-pIII fusion proteins.